REMARKS

Claims 12, 14, 15 and 39 are pending. Claim 15 has been amended. No new matter has been added and entry of the amendment is respectfully requested.

Interview

Applicants and their representative thank the Examiner and his Supervisor for the courtesy shown during the personal interview conducted on August 16, 2005. The subject matter of the interview was agreed upon and an Interview Summary was placed in the record. Although no agreement was reach, Applicants and their representative appreciate the time the Examiner and his supervisor took to discuss the issues in the present case.

Discussion of Objection to Specification

Applicants have reviewed the specification for instances where a web address was recited. The specification has been amended to remove citations to web addresses as requested by the Office.

The Invention is Useful to Treat Prostate Cancer

Claims 12, 14-15, and 39 were rejected under 35 U.S.C. § 101 because the claimed invention allegedly is not supported by either a specific and substantial asserted utility or a well established utility.

Specific Utility

The Office has alleged that Applicants have not asserted either a specific utility for the claimed invention because the biological function of the protein is not known. "[A] specific utility is particular to the subject matter claimed and would not be applicable to a broad class of invention." *In re Fisher*, 2005 U.S. App. LEXIS 19259, 18 (*citing* MPEP §2107.01). The pending claims are drawn to a composition comprising an isolated or recombinant protein of SEQ ID NO: 2.

Applicants are not asserting a broad or general utility. Instead, Applicants have asserted that this protein can be used as a therapeutic target to treat cancerous prostate cells. For the purposes of the present discussion Applicants assert that the protein is useful to target a therapeutic

compound, such as an antibody which specifically binds to the protein, to cancerous prostate cells. This antibody, for example, labeled with a radioisotope, when targeting prostate cells expressing the claimed protein, will deliver the radioisotope to the cancer cell, cause the cell to be irradiated, and ultimately die. Thus, the protein is useful for the preparation of the therapy for prostate cancer. Applicants submit that the assertion that the claimed protein is useful as a therapeutic target to treat prostate cancer is a specific utility.

Biological Function and Substantial Utility

The Office also alleged that because Applicants have not determined the biological function of the claimed protein that it lacks utility. The Office appears to be applying a *per se* rule that in the absence of knowledge of the function of a novel protein it cannot be useful. Applicants are not aware of any support, either in the statute or in the case law which supports such a *per se* rule. In the present case, the utility for the claimed protein is not derived from its function but rather that it is present in the target cell population. As such, the biological function of the protein itself is not relevant for the purposes of the invention.

Substantial Utility

A substantial utility is one that defines a "real world" or a "practical" use. MPEP §2107.01. "'Practical utility' is a shorthand way of attributing 'real-world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler,* 626 F.2d 853, 856 (C.C.P.A. 1980) Any reasonable use asserted by an applicant that provides a public benefit "should be accepted as sufficient, at least with regard to defining a 'substantial' utility." MPEP §2107.01, *see also Nelson* at 856.

In the present case, the pending claims are directed to an isolated recombinant protein comprising the amino acid sequence of SEQ ID NO: 2. Applicants have asserted in the application that the claimed protein is useful as a target for a therapeutic agent, such as an antibody, to treat prostate cancer as well as other cancers. Specification, page 3, lines 7-12. The present application contains evidence that the novel gene which encodes the target protein expresses mRNA in normal and cancerous prostate cancer cells. Specification, page 75, line 13 to page 76, line 8, see also

Figures 4 and 5. As such, this data is sufficient to support Applicants asserted utility because one of ordinary skill in the art would have a reasonable belief that protein would be expressed by the mRNA transcripts detected in the target cells. Additionally, Applicants have shown the recombinant expression of the novel. See Specification, Example 8, page 80, line 15 to page 81, line 5 and Figure 11. This data indicated that the mRNA message detected in the prostate cancer cells contains the predicted open reading frame and encodes a real protein which can serve as an antigen for producing antibodies. All of this data, taken as a whole, is more than sufficient to demonstrate to one of ordinary skill in the relevant art that the presently claimed invention is useful for the detection of prostate cancer.

As discussed above, Applicants have asserted that the protein component of the claimed composition is useful *inter alia*, as a therapeutic target for treating prostate cancer. The specification discloses that the 84P2A9 gene is expressed in prostate cancer. Based on the demonstrated expression profile, 84P2A9 proteins encoded by and translated from the detected mRNA detected in the target cells have substantial utility as prostate cancer therapeutic target.

The asserted utility is practical, based upon a well-recognized need in the art for additional prostate cancer markers, particularly those which show selective expression on prostate cancer cells over normal prostate. For example, it is well known in the art that established prostate-differentiation markers, including prostate-specific antigen (PSA), prostate-specific membrane antigen (PSMA), and prostate stem cell antigen (PSCA), are expressed in varying levels by normal prostate and in other cancers. *See, e.g.,* Reiter et al., *Proc. Natl. Acad. Sci. USA*, 95: 1735-1740 (1998), Figure 1: Northern blot comparing PSA and PSCA expression in normal prostate and LAPC cells; Schmittgen et al., *Int. J. Cancer*, 107: 323-9 (2003), Table III and discussion at page 327: PSMA expression in normal prostate was three-fold less than in prostate tumors, but the difference was not statistically significant.

In view of the data provided in the specification as well as the art-recognized need for additional prostate cancer markers, Applicants submit that the specification clearly asserts a substantial utility for the claimed invention.

Applicants Have Provided Sufficient Evidence to Support the Asserted Utility

The Office alleged in the final Office Action that the present case is analogous to *Brenner v. Manson*, 383 U.S. 519 (1966). An assertion of utility must be supported by evidence showing "a sufficient likelihood" that claimed subject matter would function as predicted. *Id.* at 532. The Federal Circuit has again restated its support for the holding in *Brenner* in the recent case of *In re Fisher*, ___ F.3d ____, 2005 U.S. App. LEXIS 19259 (Fed. Cir. 2005). While Applicants agree that the starting point for a utility analysis is *Brenner v. Manson*, that point is the beginning and the end of the relevance of *Brenner* to the present case.

In *Brenner*, the inventor has sought to patent a method for producing a novel hormone, whose sole utility was its potential role as an object of use-testing. Manson disclosed no evidence that the hormone produced by his process had any practical utility. Manson attempted to support the utility asserted in the patent application by pointing to a structurally-related hormone which had been shown to have tumor-inhibiting effects in mice. *Id.* at 531. The Office rejected this assertion indicating that there was an insufficient likelihood that the compound would have the same tumor-inhibiting properties as those related compounds disclosed. *Id.* at 532. "Indeed, respondent himself recognized that the presumption that adjacent homologues have the same utility has been challenged in the steroid filed because of 'a greater known unpredictability of compounds in that field." *Id.* The evidence cited above regarding the expression of the claimed protein on prostate cancer cells clearly distinguishes the facts of the present case from those of *Brenner.*

The Office has not stated a *prima facie* case

When making a rejection for an alleged lack of utility, the Office must make a *prima facie* showing that the claimed invention lacks utility and it must provide sufficient evidence to support the basis of that *prima facie* showing. *In re Gaubert*, 524 F.2d 1222, 1224 (CCPA 1975); MPEP § 2107.02. Applicants need only disclose a single specific and substantial utility to satisfy the requirement of the statute. *In re Fisher*, ___ F.3d ___, 2005 U.S. App. LEXIS 19259, 12 (Fed. Cir. 2005).

As evidence to support the *prima facie* showing, the Office cited a number of different publications which were alleged to support the assertion that one of ordinary skill in the relevant art

would reasonably doubt that protein is produced from a cancer cell in which mRNA for that protein has been detected. These references include Alberts, et al., Molecular Biology of the Cell, 3rd edition, 1994, page 465; Lewin, B., Genes VI, Chapter 29 (1997); Fu, *et al.*, Translational regulation of human p53 gene expression, EMBO J., 1996, 15: 4392-4401; and Mallampalli, et al., Biochem. J., 318:333-341 (1996). These references are reviewed below. As will become readily apparent, none of these references stands for the proposition that one of ordinary skill in the art would reasonably doubt the existence of at least some detectable protein expression occurring when detectable levels of mRNA are present.

The first paper cited by the Office is Alberts, et al., Molecular Biology of the Cell, 3rd edition, 1994, page 465. This section of the text discusses the post-translational control system which regulates the expression of transferrin/ferritin. The Office notes that expression of the ferritin polypeptide is blocked during iron starvation while transferrin mRNA is degraded to limit transferrin polypeptide expression. The Alberts, et al. reference neither teaches nor suggests that absolutely no transferrin or ferritin are produced. One of ordinary skill in the art would not reasonably conclude, based on the discussion of the transferrin/ferritin regulatory system provided by Alberts, et al., that absolutely no protein was produced.

The Office next cites to Lewin, B., Genes VI, Chapter 29 (1997) to support the utility rejection. The Office alleges that translation of mRNA in the cytoplasm is also a point of control for some genes. While this statement is correct, it has been taken out of context. The full quote from Chapter 29 of Lewin at page 847, second column reads:

> "Finally, the translation of an mRNA in the cytoplasm can be specifically controlled. There is little evidence for the employment of this mechanism in adult somatic cells, but it does occur in some embryonic situations, as described in Chapter 7."

When read in context, it is clear that the cytoplasmic regulation of eucaryotic genes is rare, and that there is little evidence for its use in adult somatic cells. Because the present protein is expressed in adult prostate cells, one of ordinary skill in the art would not reasonably conclude that the claimed protein was regulated in the cytoplasm.

The Office cited to the Lewin reference again for the proposition that control of gene expression can occur at multiple stages and that production of RNA cannot inevitably be equated with production of protein. The Office has again taken this statement out of context. The full quote from Chapter 29 of Lewin at page 847, second column to page 848, first column reads:

> "But having acknowledged that control of gene expression can occur at multiple stages, and that production of RNA cannot inevitably be equated with production of protein, it is clear that the overwhelming majority of regulatory events occur at the initiation of transcription."

The full citation from Lewin, rather than supporting the Office's position instead undermines it. One of ordinary skill in the art, reading this passage would reasonably conclude that once a gene is transcribed, it is more likely than not that the mRNA will be translated to produce protein.

The most interesting paper cited by the Office was Fu, et al., Translational regulation of human p53 gene expression, EMBO J., 1996, 15: 4392-4401. Fu, et al. teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation.

Lack of a direct correlation between mRNA levels and protein levels does not support the position taken by the Office that the art recognizes that even when detectable levels mRNA are present that there are circumstances when absolutely no protein is made from that mRNA. Even this paper where mRNA was detected but no protein could be found in some of the samples does not support the position of the Office. As discussed by Fu, et al., the inability to detect p53 protein in certain samples was likely to be due to forms of p53 which extremely short half-lives, as discussed in Rogel, et al., "p53 cellular tumor antigen: analysis of mRNA levels in normal adult tissues, embryos, and tumors," (Mol Cell Biol. 1985 Oct;5(10):2851-5).

The final paper cited by the Office was Mallampalli, et al., Biochem. J., 318:333-341 (1996). This paper showed that treatment of a test system with glucocorticoid and beta-methasone increased mRNA expression levels of cytidylyltransferase (CT) but levels of the CT enzyme were not increased.

The results disclosed in this paper can be explained by noting that RT-PCR and Southern analysis are more sensitive than Western blot analysis. Thus, the detection methods used may have biased the results in favor of detecting mRNA expression and away from detecting protein expression. Regardless, however, this paper does not stand for the proposition that the presence of detectable mRNA levels frequently, commonly or inevitably fail to produce protein.

The papers discussed above notwithstanding, the relevant question is at hand is whether one of ordinary skill in the art could reasonably conclude that when mRNA is detected, it is more likely than not that that mRNA is translated into protein which could then be detected by the claimed antibody. The Office argued that the papers cited show that mRNA expression cannot inevitably be equated with protein production. Inevitability is not the test for utility. All that Applicants need to show is that one of ordinary skill in the art could reasonably conclude based on the evidence presented in the specification, that mRNA detected would produce protein.

The specification has demonstrated that the relevant mRNA is present and expressed in prostate cancer cells. Thus, the claimed protein is useful as a therapeutic target for targeting therapeutic molecules, such as antibodies to prostate cancer cells. In view of the discussion above, Applicants respectfully submit that the Office has failed to articulate a *prima facie* showing to support the allegation that the pending claims lack a specific, substantial and well-defined utility. As such, Applicants request that the present rejection be withdrawn.

Applicants submit by declaration additional evidence of utility for the claimed invention

In addition to the data provided in the specification and the failure of the Office to articulate a *prima facie* case of lack of utility, Applicants submit herewith additional evidence demonstrating that the protein of interest is detectable in tumor samples. This evidence is provided in the form of a Rule 1.132 declaration by Dr. Karen Morrison, one of the named inventors for the present case.

The data provided in the declaration shows unequivocally that the protein of interest is expressed in prostate cancer, and that the protein can be detected by immunochemistry. In addition to prostate cancer, the data provided shows that the protein is expressed in lung cancer and that the protein can be detected in lung cancer. In view of these showings, it is apparent that 84P2A9

protein can be used to elicit the production of antibodies immunoreactive with 84P2A9 protein, are useful in detecting the presence of cancer.

The claimed invention is useful

The remarks and evidence provided above are sufficient to support Applicants assertion that the claimed subject matter is useful. As such and in view of the fact that the Office has failed to assert a *prima facie* case of lack of utility, Applicants request that the present rejection be withdrawn.

Discussion of Rejection Under 35 U.S.C. § 112

Claim 15 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Claim 15 was also rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Both rejections were based on language in claim 15 which recited a polynucleotide that selectively hybridized to a specified nucleotide. While Applicants respectfully disagree with the Office's reasoning regarding the rejections of claim 15, this claim has been amended to delete the hybridization language rejected by the Office. As such, the reasons for the rejections of claim 15 have been eliminated. Thus, these rejections should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 511582000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: October 12, 2005

Respectfully submitted,

By _____

James J. Mullen III, Ph.D.
Registration No.: 44,957
MORRISON & FOERSTER LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
(858) 720-7940